REMARKS

Favorable reconsideration of the subject application as amended above and further in view of the comments below is respectfully requested.

Claims 1-21 are pending in the present application. Claims 6, 15 and 19 are canceled herein, and new claims 22 and 23 have been added. Accordingly, claims 1-5, 7-14, 16018 and 20-23 are presented for examination on the merits.

The amendments to the claims were made to make that which was implicit in the original claims explicit. Claim 1 has been amended to more particularly define the claimed method as a method for assessing the effectiveness of a therapeutic agent. The claim was also amended to more particularly define the step of assaying for protein in the sample. Support for the amendments to claim 1 is found at page 15.

New claim 22 is directed to a preferred embodiment where native and intact albumin are detected in the sample. Support for this amendment is found throughout the specification and original claims.

New claim 23 is directed to a preferred embodiment where an antibody assay is used in the claimed method.

I. Objection to the Disclosure

It is respectfully submitted that the objection to the disclosure is respectfully rendered moot by the amendment thereto.

II. Rejection of Claims 1-19 Under 35 U.S.C § 112, Second Paragraph

Claims 1-19 are rejected under 35 U.S.C § 112, second paragraph as being indefinite for failing to point out and distinctly claim the subject matter that applicant regards as the invention

This rejection is respectfully rendered moot by the amendment to claim 1.

III. Rejection of Claims 1-7, 16-17 and 20 Under 35 U.S.C § 102(b)

Claims 1-7, 16, 17 and 20 are rejected under 35 U.S.C § 102(b) as being anticipated by Trevisan et al.

This rejection is respectfully rendered moot by the amendments to the claims.

IV. Rejection of Claims 18, 19 and 21 Under 35 U.S.C § 103(a)

Claims 18, 19 and 21 are rejected under 35 U.S.C § 103(a) as being unpatentably obvious over Trevisan in view of Suzuki et al. The Examiner states that Trevisan discloses administration of rampiril and assaying for the effects of the drug on microalbuminuria over a period of six months by measuring urinary albumin content by RIA. The Examiner relies on Jain et al. as teaching detection of albumin with an albumin-specific dye. (It appears that the Examiner mistakenly omitted Jain et al. from the rejection, since Jain et al. is relied upon). Suzuki et al. is relied upon as teaching that detection of urinary microalbuminuria indicates early stage nephropathy. The Examiner concludes, therefore, that it would have been obvious to detect early-stage renal disease with Trevisan's method.

This rejection is respectfully traversed as follows.

The present invention is directed to a method of assessing a treatment for renal disease or complications of renal disease wherein both native and intact modified protein are detected in a urine sample. Applicant has discovered that conventional assays for detecting protein in urine, such as albumin, fail to detect all forms of the protein that may be present. As a result, conventional methods fail to detect a protein imbalance until the pathological condition has progressed to a point where the kidneys are actually irreversibly damaged. Applicant's studies have shown that when the kidneys are not functioning properly, e.g., as a result of kidney disease, the urine contains both intact and intact modified proteins, as well as fragmented proteins. However, the intact modified proteins are not typically detected by conventional screening methods, such as RIA. Consequently, kidney disease cannot be diagnosed until enough of the intact (native) protein is present in the urine to be detected, which most often does not occur until the later stages of disease when irreversible kidney damage has already occurred. (spec. p. 3, para. 3).

Applicant has developed an assay to determine the effectiveness of an agent for the treatment of renal disease or renal complications of a disease, which includes measuring both intact native and intact modified protein. Consequently renal disease and renal complications of disease can be detected significantly earlier with Applicant's method and the effectiveness of treatment can be more accurately determined than with conventional assays that detect only native protein in the urine.

The prior art relied on by the Examiner merely teaches the use of conventional assays, for example, RIA, for detecting intact albumin in urine. The cited prior art does not teach or suggest that modified intact protein is present in urine, or that the presence

of intact modified protein correlates to the presence of renal disease or renal complications of disease. Instead, the combined prior art merely teaches measurement of native albumin by conventional assays. As such, the cited combination of prior art does not render the present invention obvious.

Accordingly, the rejection of claims 18, 19 and 21 under 35 U.S.C § 103(a) is respectfully traversed.

It is respectfully submitted that the present application, as amended above, is in condition for allowance, an early notification thereof being earnestly submitted.

To the extent necessary, a petition for an extension of time under 37 C.F.R. § 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such account.

Respectfully submitted,

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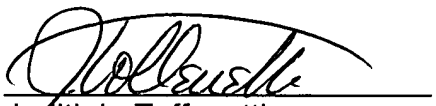
Date: Dec. 9, 2002 By: 

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MARKED UP VERSION SHOWING CHANGES MADE

Please *cancel claims 6, 15 and 19.*

Please amend claims 1, 7, 8, 9, 10, 11, 13, 14, 20 and 21 and add new claim 22 as follows:

Claim 1 (Amended). A method for [treating] assessing therapeutic effectiveness of a treatment agent for [a person with a] renal disease and/or renal complications of a disease, comprising:

(a) administering a treatment agent to [a person in need thereof] a patient;

(b) obtaining a urine sample [of body fluid] from the [person] patient;

(c) assaying for a protein in the urine sample by detecting the native protein and intact modified form of the protein in the urine sample,

wherein [either] presence of or lack of [presence of] the protein in the urine sample or decreasing amount of the protein over time in the urine [indicates that the treatment agent is therapeutically effective for the renal disease and/or the renal complications of a disease] correlates with effectiveness of the treatment agent.

Claim 7 (Amended). The method [according to] of claim 1, wherein the protein [comprises] is selected from the group consisting of albumin, globulin, [(] alpha-globulin, [(] $alpha_1$-globulin, $alpha_2$-globulin[)], beta-globulin, gamma-globulin, euglobulin, pseudoglobulin I and II, fibrinogen, $alpha_1$ acid glycoprotein (orosomucoid), $alpha_1$ glycoprotein, $alpha_1$ lipoprotein, ceruloplasmin, $alpha_2$ 19S glycoprotein, $beta_1$ transferrin, $beta_1$ lipoprotein, immunoglobulins A, E, G and M, horseradish peroxidase,

lactate dehydrogenase, glucose oxidase, myoglobin, lysozyme, protein hormone, growth hormone, insulin[, or] and parathyroid hormone.

Claim 8 (Amended). The method according to claim 1, wherein the assaying for a protein in the urine sample comprises [a method selected from the group consisting of:

(a) assaying for albumin by a conventional method; and

(b)] assaying for native and intact modified albumin.

Claim 9 (Amended). The method according to claim 8, wherein the [conventional method] assaying comprises [a method selected from the group consisting of] :

(a) an antibody method, and

(b) a non-antibody method comprising [loading the sample on a] chromatography, electrophoresis or sedimentation [apparatus] of the sample to test for the presence of native or intact modified albumin.

Claim 10 (Amended). The method [according to] of claim 9, wherein the albumin is detected by an antibody or antibodies [that is] specific for both unmodified and modified forms of [the protein] albumin.

Claim 11 (Amended). The method according to claim 9, wherein the albumin is detected by an antibody that is specific for the modified [protein] albumin.

Claim 13 (Amended). The method according to claim 1, wherein the assaying for a protein in the sample comprises the steps of:

(i) detecting the native [albumin] protein amount by conventional antibody assay[:]; and

(ii) detecting the native plus intact modified [albumin] protein by a non-antibody method[; and

(iii) adding the values obtained in (i) and (ii) to obtain an accurate reading of total albumin content in the sample].

Claim 14 (Amended). The method according to claim 13, wherein the non-antibody method comprises [loading the sample on a] chromatography, electrophoresis or sedimentation of the sample [apparatus] to test for native or intact modified [albumin].

Claim 20 (Amended). A method for identifying a treatment agent for renal disease and/or renal complications of a disease, comprising:

(a) administering a candidate therapeutic agent to a [person in need thereof] patient [an agent that is suspected of being able to treat the disease];

(b) obtaining a series of urine [sample] samples from the [person] patient over time; and

(c) assaying for a protein in each of the [sample,] samples in the series of samples by a non-antibody assay or an antibody assay which measures both native form of the protein and intact modified form of the protein.

wherein [either presence of or lack of presence of the protein in the urine or] a decreasing amount of the protein over time in the urine indicates that the candidate therapeutic agent is a treatment agent for the renal disease and/or the renal complications of a disease.

Claim 21 (Amended). The method of claim 19, wherein [the] assaying for a protein in the [sample] samples comprises assaying for a modified form of albumin [in the sample], wherein [either presence of or a lack of presence of the modified form of the protein in the sample or] decreasing amount of the modified form of the [protein] albumin over time in the urine indicates that the candidate therapeutic agent is a treatment agent for the renal disease and/or the renal complications of a disease.

Please add the following new claim:

Claim 22 (New). The method according to claim 13 wherein the protein is albumin.

Claim 23 (New). The method of claim 20 wherein an antibody assay is used in step (c).